

## Click reactions in the synthesis of tripodal 1H-1,2,3-triazol derivatives of 1,3,5-triazinane-2,4,6-trione

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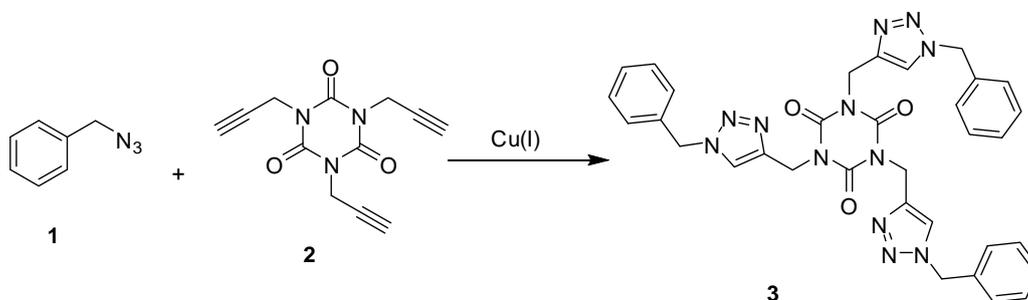
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*Abstract: The copper catalyzed Huisgen's reaction was used for the synthesis of two derivatives of 1H-1,2,3-triazol-1,3,5-triazinane-2,4,6-trione. One from tris(2-azidoethyl)-1,3,5-triazinane-2,4,6-trione and phenylacetylene, and the other by coupling of 1,3,5-tri(prop-2-yn-1-yl)-1,3,5-triazinane-2,4,6-trione with benzyl azide.*

Copper catalyzed Huisgen's reaction is a widespread tool in click chemistry.<sup>1</sup> However there are few examples about its use in the building of molecules based in a isocyanuric acid core with C<sub>3</sub> symmetry.<sup>2,3</sup>

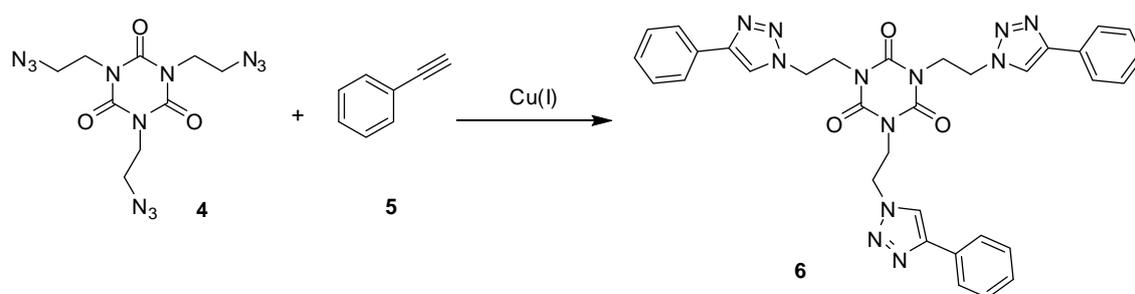
In order to establish the achievability and conditions of this reaction to prepare this sort of compounds, we studied the reaction with a commercial azide (benzylazide, **1**) and the alkyne **2**,<sup>4</sup> synthesized from cyanuric acid **3**.

Then, to obtain triazole **3** (Scheme 1), alkyne, benzylazide, copper(II) sulfate and sodium ascorbate, in 1:3,5:0,5:1 proportions, were mixed in DMF/water. The reaction was left at room temperature for 24 h. Once no starting alkyne was detected by TLC, water and ethyl acetate were added, appearing a solid. This was isolated by filtration (60% yield) and the <sup>1</sup>H NMR spectrum confirmed the structure of **3**. It showed a singlet at δ 7.50 ppm corresponding to the triazole ring hydrogen, aromatic hydrogens (δ 7.27 to 7.18 ppm) and two singlets assigned to the two CH<sub>2</sub> groups (δ 5.39 and 5.05 ppm). In addition the mass spectrum shows a peak at m/z 665 corresponding to the molecular ion plus sodium.



Scheme 1.

To see the scope of the reaction, the same method was used to synthesize the triazole **6** (Scheme 2), using as reagents the azide **4**<sup>5</sup> and phenylacetylene. The reaction was carried out under the conditions described above and analyzed by TLC (after 24 h starting azide disappeared). From the reaction mixture a solid was separated by filtration and it was identified as **6** (67% yield).



Scheme 2.

The spectroscopic data were consistent with this structure. The mass spectrum showed the molecular ion plus sodium at  $m/z$  665. The  $^1\text{H}$  NMR spectrum displayed a singlet at  $\delta$  8.46 ppm of hydrogen in the triazole ring, aromatic hydrogens signals ( $\delta$  7.81 to 7.29 ppm) and two triplets at  $\delta$  4.53 and 4.17.

Both tripodal compounds were minimized with MOPAC 2009<sup>7</sup> using Hamiltonian PM6, the resulting structures indicate that triazole **6** is more planar than **3**, due to the conjugation of triazole and benzene rings (Figure 1).

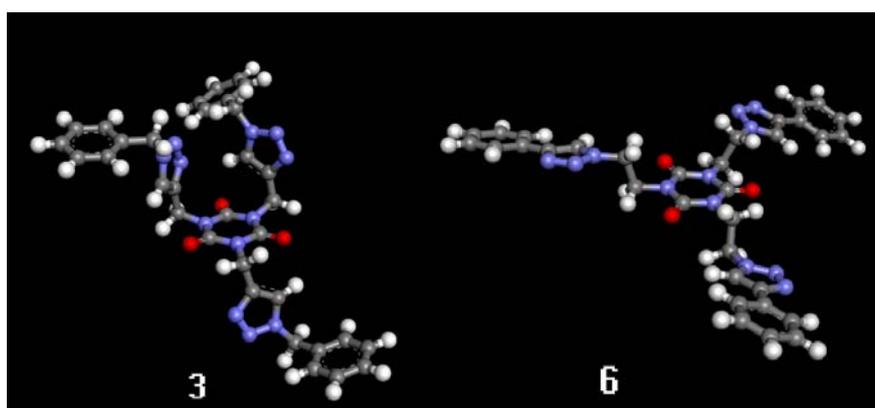


Figure 1.

In summary, the feasibility of the synthesis of tripodal 1H-1,2,3-triazol derivatives of 1,3,5-triazinane-2,4,6-trione by Huigen's reaction was demonstrated. These compounds would have potential suitability as stabilizing ligands for metals in catalysis.<sup>6</sup>

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## General procedure

Synthesis of tris[(1-benzyl-1H-1,2,3-triazole-4-yl)methyl]-1,3,5-triazinane-2,4,6-trione (**3**). Alkyne **2** (300 mg, 1.23 mmol), benzylazide (575 mg, 4.32 mmol) and sodium ascorbate (245 mg, 1.23 mmol) were dissolved in DMF (4 mL). Dropwise was added a solution of copper(II) sulfate (154 mg, 0.615 mmol) in water (2 mL), and left 24 hours at room temperature in an inert atmosphere. DMF was evaporated and water (100 mL) and ethyl acetate (100 mL) were added, a solid appeared and it was filtered. The solid was washed with ethyl acetate and dried under vacuum. This gives the triazole **3** (475 mg, 60%) as a pale green solid. M.p. 183-184 °C. RMN <sup>1</sup>H (300 MHz, CDCl<sub>3</sub>) δ 7.50 (s, 3H, NCH), 7.26 (br s, 9H, ArH), 7.19 (d, 6H, ArH, J<sub>ortho</sub> = 7.5 Hz), 5.39 (s, 6H, CH<sub>2</sub>Ph), 5.05 (s, 6H, CH<sub>2</sub>NCO). RMN <sup>13</sup>C (300 MHz, CDCl<sub>3</sub>) δ 148.6 (C=O), 142.6 (C-N=N), 134.7 (quaternary Ph), 129.3, 129.0, 128.4 (CH, Ph), 123.6 (CH-N), 54.4 (CH<sub>2</sub>Ph), 38.2 (CH<sub>2</sub>NCO). IR (goldengate, cm<sup>-1</sup>): 1690 (C=O), 1452, 1423, 1229, 1076, 764, 756, 696. MS (ES) m/z (%): 665 (M<sup>+</sup>+Na, 84), 235 (48), 131 (93), 101 (57), 77 (100).

## References

1. *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; A. Padwa, W. H. Pearson eds.; John Wiley & Sons, 2002.
2. Liu, Y.; Díaz, D. D.; Accurso, A. A.; Sharpless, K. B.; Fokin, V. V.; Finn, M. G. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 5182-5189.
3. Sugai, N.; Heguri, H.; Ohta, K.; Meng, Q.; Yamamoto, T.; Tezuka, Y. *J. Am. Chem. Soc.* **2010**, *132*, 14790-14802.
4. Grigoryan, S. G.; Avetisyan, K. G.; Arzumanyan, A. M.; Mardoyan, M. K.; Matnishyan, A. A. *Khimicheskaya Promyshlennost, Seriya: Reaktivy i Osobo Chistye Veshchestva* **1981**, *3*, 34-5. *Chem. Abstr. Scifinder* AN1982:68948 CAN 96:68948.
5. Hettche, F.; Hoffmann, R. W. *New J. Chem.* **2003**, *27*, 172-177.
6. Chan, T. R.; Hilgraf, R.; Sharpless, K. B.; Fokin, V. V. *Org. Lett.* **2004**, *6*, 2853-2855.
7. Stewart, J. J. P. Stewart Computational Chemistry, Version 11.052W, web: [HTTP://OpenMOPAC.net](http://OpenMOPAC.net)